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STRUCTURE FILE UPDATES: 12 JUL 2009 HIGHEST RN 1161919-42-1 DICTIONARY FILE UPDATES: 12 JUL 2009 HIGHEST RN 1161919-42-1

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http://www.cas.org/support/stngen/stndoc/properties.html

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    ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
T.1
RN
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    Entered STN: 08 Sep 2000
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CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

OTHER NAMES:

CN 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline

CN AZD 2171

CN Cediranib

CN ZD 2171

DR 790713-41-6, 557795-03-6

MF C25 H27 F N4 O3

CI COM

SR CA

LC STN Files: ADISINSIGHT, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

87 REFERENCES IN FILE CA (1907 TO DATE)

5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

87 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 7.88 8.10

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 13:30:39 ON 13 JUL 2009
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FILE COVERS 1907 - 13 Jul 2009 VOL 151 ISS 3
FILE LAST UPDATED: 12 Jul 2009 (20090712/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2009

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> 11

L2 87 L1

=> 12 and py<2005

25140894 PY<2005

L3 5 L2 AND PY<2005

=> d 13 ibib abs 1-5

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:995977 CAPLUS

DOCUMENT NUMBER: 141:420417

TITLE: Therapeutic agents comprising an anti-angiogenic agent

in combination with an Src inhibitor for use in

normotensive treatment of angiogenesis

INVENTOR(S): Curwen, Jon Owen; Wedge, Stephen Robert

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT	NO.			KIN:	D	DATE			APPL	ICAT	ION :	NO.	DATE				
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NO 2005004411	A	20051130	ИО	2005-4411		20050923
ZA 2005008858	А	20070328	ZA	2005-8858		20051101
US 20060223815	A1	20061005	US	2005-555389		20051103
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PRIORITY APPLN. INFO.:			GB	2003-10401	A	20030507
			WO	2004-GB1939	W	20040504

GΙ

AΒ The invention relates to the use of an anti-angiogenic agent, such as I (preparation given), in combination with an inhibitor of the Src family of non-receptor tyrosine kinases, such as the II (prepns. according to a previous patent given), in the manufacture of a medicament for use in the substantially normotensive treatment in a warm-blooded mammal such as a human being of a disease state associated with angiogenesis. The invention provides for the Src kinase inhibitor to be administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent. Thus, 7-(2-chloroethoxy)-4-(6-chloro-2,3methylenedioxyanilino)-5-isopropoxyquinazoline was coupled with 1-acetylpiperazine using KI in DMA to give I. The diastolic blood pressure profile of rats over a 24 h period after administration of a combination of 1.5 mg/kg of I and 25 mg/kg of II demonstrated that the contrasting blood pressure effects of the antiangiogenic agent and the Src kinase inhibitor were substantially counterbalanced.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:965067 CAPLUS

DOCUMENT NUMBER: 141:406039

TITLE: Combinations for the treatment of diseases involving

cell proliferation, migration or apoptosis of myeloma

cells, or angiogenesis

INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin

Friedrich; Baum, Anke; Munzert, Gerd; Van Meel,

Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;

Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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       WO 2004096224
                                  A3 20041216
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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                                          20060425 BR 2004-9919
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PRIORITY APPLN. INFO.:
                                                              EP 2003-9587
                                                                                        A 20030429
                                                              EP 2004-508
                                                                                        A 20040113
                                                              EP 2004-1171
                                                                                         A 20040121
                                                              WO 2004-EP4363 W 20040424
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AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2003:532545 CAPLUS

DOCUMENT NUMBER: 139:95455

TITLE: Combined therapy against tumors comprising substituted

acryloyl distamycin derivatives and protein kinase

(serine/threonine kinase) inhibitors

INVENTOR(S): Geroni, Maria Cristina; Fowst, Camilla; Cozzi, Paolo

PATENT ASSIGNEE(S): Pharmacia Italia SpA, Italy

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	TENT NO.	KIN	D DATE	APPLICATION NO.	DATE
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ES	2263835	T3	20061216	ES 2002-787763	20021218
NZ	533854 2328306 2004006543 2004005290	A	20070531	NZ 2002-533854 RU 2004-123641 MX 2004-6543	20021218
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irb ca	OURCE(S):	MvD.	DAT 130.05/5		A3 20040/00
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GΙ

AB The present invention provides the combined use of acryloyl distamycin derivs., in particular α -bromo- and α -chloro-acryloyl distamycin derivs., and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis. An example protein kinase inhibitor is STI 571 and a distamycin derivative is brostallicin (I).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:747609 CAPLUS

DOCUMENT NUMBER: 135:283196

TITLE: Therapeutic combinations of antihypertensive and

antiangiogenic agents

INVENTOR(S): Curwen, Jon Owen; Ogilvie, Donald James

PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 2001074360	A1 200110	011 WO 2001-GB1522	20010402 <
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      WO 2001-GB1522
      W 20010402

      KR 2002-713170
      A3 20021002

OTHER SOURCE(S):
                                    MARPAT 135:283196
        The invention concerns the use of a combination of an anti-angiogenic
        agent and an anti-hypertensive agent for use in the manufacture of a medicament
        for the treatment of a disease state associated with angiogenesis in a
        warm-blooded mammal, such as a human being. The invention also relates to
        pharmaceutical compns. comprising an anti-angiogenic agent and an
        anti-hypertensive agent, to kits thereof and to a method of treatment of a
        disease state associated with angiogenesis which comprises the administration
        of an effective amount of a combination of an anti-angiogenic agent and an
        anti-hypertensive agent to a warm-blooded animal, such as a human being.
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blood pressure was reversed by the addition of captopril.

REFERENCE COUNT:

3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ylmethoxy)quinazoline for 10 days, then they were dosed orally with 30

mg/kg captopril in addition to quinazoline compound The increase in diastolic

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2000:573671 CAPLUS

Anesthetized rats were dosed orally with 12.5 mg/kg of

4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-

DOCUMENT NUMBER: 133:177183

TITLE: Preparation of quinazoline derivatives as angiogenesis

inhibitors

INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick;

Stokes, Elaine Sophie Elizabeth; Mckerrecher, Darren

PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Zeneca-Pharma S.A.

SOURCE: PCT Int. Appl., 346 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

	KIND DATE	APPLICATION NO.	
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OTHER SOURCE(S):

MARPAT 133:177183

GΙ

$$Z-A-(R^1)_n$$
 $R^2)_m$
 R^2
 R^3
 R^3

The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered AΒ bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z = O, NH, S, CH2, or a bond; n = 0-5; m = 0-3; R2 = H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1 = a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5 = H or (un)substituted alkyl, alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or (alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

REFERENCE COUNT:

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 13 ibib abs 1-5 hitstr

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2004:995977 CAPLUS

DOCUMENT NUMBER: 141:420417

TITLE: Therapeutic agents comprising an anti-angiogenic agent

in combination with an Src inhibitor for use in

normotensive treatment of angiogenesis Curwen, Jon Owen; Wedge, Stephen Robert

INVENTOR(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited PATENT ASSIGNEE(S):

PCT Int. Appl., 111 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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	20060							1005				5553						
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									•	WO 2	004-0	GB19:	39	1	W 2	0040	504	

AΒ The invention relates to the use of an anti-angiogenic agent, such as I (preparation given), in combination with an inhibitor of the Src family of non-receptor tyrosine kinases, such as the II (prepns. according to a previous patent given), in the manufacture of a medicament for use in the substantially normotensive treatment in a warm-blooded mammal such as a human being of a disease state associated with angiogenesis. The invention provides for the Src kinase inhibitor to be administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent. Thus, 7-(2-chloroethoxy)-4-(6-chloro-2,3methylenedioxyanilino)-5-isopropoxyquinazoline was coupled with 1-acetylpiperazine using KI in DMA to give I. The diastolic blood pressure profile of rats over a 24 h period after administration of a combination of 1.5 mg/kg of I and 25 mg/kg of II demonstrated that the contrasting blood pressure effects of the antiangiogenic agent and the Src kinase inhibitor were substantially counterbalanced.

IT 288383-20-0, 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (angiogenesis inhibitor; therapeutic agents comprising an anti-angiogenic agent in combination with an Src inhibitor for use in normotensive treatment of angiogenesis)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

$$N-(CH_2)_3-O$$
 MeO
 N
 F
 N
 MeO
 N
 M
 M
 M
 M

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:965067 CAPLUS

DOCUMENT NUMBER: 141:406039

TITLE: Combinations for the treatment of diseases involving

cell proliferation, migration or apoptosis of myeloma

cells, or angiogenesis

INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin

Friedrich; Baum, Anke; Munzert, Gerd; Van Meel,

Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;

Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

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73 17 1		IE,	SI,	LT,	LV,	FI,	RO,	FR, MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK	•	
CA	2004 2523 1622	868			A1		2004	1111		CA 2	004-	2523	868		2	0040	424	
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JP MX	BR 2004009919 JP 2006524634 MX 2005011656				T A		2006 2005	1102 1215		JP 2 MX 2	006- 005-	5000 1165	99 6		2 2	0040 0040 0051 0051	424 028	
	NO 2005005605 CORITY APPLN. INFO.:						2000	1120		EP 2	003- 003- 004-	9587				0030	429	

EP 2004-1171 A 20040121 WO 2004-EP4363 W 20040424

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

IT 288383-20-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine kinase receptor antagonists and radiotherapy)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:532545 CAPLUS

DOCUMENT NUMBER: 139:95455

TITLE: Combined therapy against tumors comprising substituted

acryloyl distamycin derivatives and protein kinase

(serine/threonine kinase) inhibitors

INVENTOR(S): Geroni, Maria Cristina; Fowst, Camilla; Cozzi, Paolo

PATENT ASSIGNEE(S): Pharmacia Italia SpA, Italy

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PAT	PATENT NO.				KIN	D	DATE			APPL	ICAT	ION I	NO.		D.	ATE	
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PRIORITY APPLN. INFO.:
                                                                 A 20020102
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OTHER SOURCE(S):
                        MARPAT 139:95455
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Br H2C=C-CO-NH Me CO-NH Me CO-NH Me CO-NH Me CO-NH-CH2 CH2 NH-C-NH2 NH

GΙ

AΒ

The present invention provides the combined use of acryloyl distamycin

derivs., in particular α -bromo- and α -chloro-acryloyl distamycin derivs., and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis. An example protein kinase inhibitor is STI 571 and a distamycin derivative is brostallicin (I).

IT 288383-20-0, ZD 2171

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combined antitumor therapy comprising acryloyl distamycin derivs. and protein kinase (serine/threonine kinase) inhibitors)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:747609 CAPLUS

DOCUMENT NUMBER: 135:283196

TITLE: Therapeutic combinations of antihypertensive and

antiangiogenic agents

INVENTOR(S): Curwen, Jon Owen; Ogilvie, Donald James

PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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OTHER SOURCE(S): MARPAT 135:283196

The invention concerns the use of a combination of an anti-angiogenic agent and an anti-hypertensive agent for use in the manufacture of a medicament for the treatment of a disease state associated with angiogenesis in a warm-blooded mammal, such as a human being. The invention also relates to pharmaceutical compns. comprising an anti-angiogenic agent and an anti-hypertensive agent, to kits thereof and to a method of treatment of a disease state associated with angiogenesis which comprises the administration of an effective amount of a combination of an anti-angiogenic agent and an anti-hypertensive agent to a warm-blooded animal, such as a human being. Anesthetized rats were dosed orally with 12.5 mg/kg of 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4ylmethoxy)quinazoline for 10 days, then they were dosed orally with 30 mg/kg captopril in addition to quinazoline compound The increase in diastolic blood pressure was reversed by the addition of captopril. ΤT 288383-20-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic combinations of antihypertensive and antiangiogenic agents)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:573671 CAPLUS

DOCUMENT NUMBER: 133:177183

TITLE: Preparation of quinazoline derivatives as angiogenesis

inhibitors

INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick;

Stokes, Elaine Sophie Elizabeth; Mckerrecher, Darren

PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Zeneca-Pharma S.A.

SOURCE: PCT Int. Appl., 346 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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	2000																	<
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EP	1154	774			A1		2001	1121	:	ΕP	2000-	-9027	30		2	0000	208	<
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CN	1597	667			А		2005		(CN	2004-	-1005	8982		2	0000	208	
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	5308	32			A						2000-							
	1553	097			ΑI						2005-							
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AT	298237		Τ	20050715	AT 2000-902730		20000208	
RU	2262935		C2	20051027	RU 2001-124816		20000208	
ES	2242596		Т3	20051116	ES 2000-902730		20000208	
IL	144745		A	20081103	IL 2000-144745		20000208	
EP	2050744		A1	20090422	EP 2008-168638		20000208	
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IN	2000DE00115	5	A	20050311			20000211	
IN	2001MN00893	3	A	20070525	IN 2001-MN893		20010726	
ZA	2001006340		A	20021101	ZA 2001-6340		20010801	<
NO	2001003882		Α	20011009	NO 2001-3882		20010809	<
NO	321604		В1	20060612				
MX	2001008182		Α	20030820	MX 2001-8182		20010810	<
KR	838617		В1	20080616	KR 2001-710133		20010810	
HK	1041212		A1	20051202	HK 2002-102781		20020412	
US	7074800		В1	20060711	US 2002-913020		20020506	
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US	20060004017	7	A1	20060105	US 2005-169122		20050629	
HK	1076104		A1	20081031	HK 2005-108262		20050921	
JP	2006273860		Α	20061012	JP 2006-129249		20060508	
KR	2008015482		А	20080219	KR 2007-731001		20071231	
PRIORITY	APPLN. INE	FO.:			EP 1999-400305	A	19990210	
					EP 2000-902730	А3	20000208	
					EP 2005-4285	А3	20000208	
					JP 2000-598164	А3	20000208	
					WO 2000-GB373	W	20000208	
					KR 2001-710133	А3	20010810	
					US 2002-913020	А3	20020506	
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OTHER SOURCE(S): MARPAT 133:177183 GI

AB The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z=0, NH, S, CH2, or a bond; n=0-5; m=0-3; R2=H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1=a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5=H or (un)substituted alkyl,

alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or (alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

IT 288383-20-0P, 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(angiogenesis inhibitor; preparation of quinazolines as angiogenesis inhibitors by cyclization of 2-aminobenzamides and subsequent derivatization)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT